

Claims

1. A method of modulating an immune system response to an antigen, the method comprising steps of:

identifying an individual who has been or will be exposed to an antigen; and

administering to the individual, concurrently with exposure to the antigen, a composition comprising at least one factor selected from the group consisting of cytokines and inducing agents, which factor is selected to bias the individual's immune response to the antigen away from a Th1 or Th2 response in a predetermined manner.

2. The method of claim 1, wherein:

the step of identifying comprises identifying an individual who is allergic to the antigen;

and

the step of administering comprises administering a composition comprising at least one factor selected to bias the individual's immune response to the antigen away from a Th2 response.

3. The method of claim 2, wherein:

the step of identifying comprises identifying an individual who has previously mounted a Th2 response to the antigen.

4. The method of claim 2, wherein:

1 the factor comprises a Th1 stimulating cytokine.

2  
3 5. The method of claim 2, wherein:

4 the factor is selected from the group consisting of IL-12, IL-2, IL-18, IL-1 $\beta$ , fragments of  
5 IL-1 $\beta$ , IFN $\alpha$ , and IFN $\gamma$ .

6  
7 6. The method of claim 2, wherein:

8 the factor comprises a Th2 stimulating cytokine.

9  
10 7. The method of claim 2, wherein:

11 the factor is selected from the group consisting of LPS, CD40, CD40 ligand, BCGs,  
12 oligonucleotides containing CpG motifs, TNF $\alpha$ , and microbial extracts.

13  
14 8. The method of claim 7, wherein:

15 the microbial extracts are selected from the group consisting of any *Staphylococcus*  
16 *aureus* preparation, heat killed *Listeria*, and modified cholera toxin.

17  
18 9. The method of claim 4, wherein:

19 the step of administering comprises delivering the factor to the vicinity of T cells.

20  
21 10. The method of claim 7, wherein:

1 the step of administering comprises delivering the factor to the vicinity of a pAPC that  
2 will internalize and display antigen to T cells.

3  
4 11. The method of claim 1, further comprising a step of:  
5 administering the antigen to the individual.

6  
7 12. The method of claim 11, wherein:  
8 the step of administering the antigen comprises administering a crude antigen preparation.

9  
10 13. The method of claim 11, wherein:  
11 the step of administering the antigen comprises administering a substantially pure  
12 antigen.

13  
14 14. The method of claim 11, wherein:  
15 the antigen is a polypeptide antigen; and  
16 the step of administering the antigen comprises administering a gene encoding the  
17 antigen, so that the gene becomes expressed within the individual.

18  
19 15. The method of claim 14, wherein:

1 the step of administering comprises administering at least one factor that is a protein, and  
2 further comprises delivering the protein factor by administering to the individual a gene encoding  
3 that factor.

4  
5 16. The method of claim 2, wherein:

6 the steps of administering the antigen and administering the composition are performed  
7 together and comprise administering a single nucleic acid construct including genes for antigen  
8 and protein factor.

9  
10 17. The method of claim 4, wherein:

11 the step of administering the single nucleic acid construct comprises administering a  
12 construct in which the antigen gene and protein factor gene are linked to one another so that a  
13 single fusion protein, containing both antigen and protein factor, is encoded.

14  
15 18. The method of claim 2, wherein:

16 the antigen gene and the factor gene are provided on separate nucleic acid molecules.

17  
18 19. The method of claim 2 or claim 18, wherein:

19 the antigen gene and the factor gene are coordinately regulated.  
20

1 20. The method of claim 1 wherein the factor is administered in association with a targeting  
2 agent.

3  
4 21. The method of claim 11 wherein one or both of the antigen and the factor is encapsulated.

5  
6 22. The method of claim 11, wherein:

7 the steps of administering the antigen and administering the composition are performed  
8 together and comprise administering the antigen and composition in association with one  
9 another.

10  
11 23. The method of claim 22, wherein:

12 the antigen and factor are administered in association with a targeting agent.

13  
14 24. The method of claim 20 or claim 23, wherein:

15 the targeting agent association occurs by means of an interaction selected from the group  
16 consisting of covalent bonds, hydrophobic interactions, van der Waals interactions, and  
17 combinations thereof.

18  
19 25. The method of claim 23, wherein:

20 the targeting agent is selected from the group consisting of mannose receptor ligand and  
21 the Fc receptor ligand.

1 26. The method of claim 29, wherein:

2 the targeting agent comprises complement receptor ligand.

4 27. The method of claim 23, wherein:

5 the targeting agent comprises DEC205.

7 28. The method of claim 23, wherein:

8 the targeting agent comprises a ligand that interacts with a receptor on an intracellular  
9 vesicle within a pAPC.

11 29. The method of claim 23, wherein:

12 the targeting agent comprises at least the Fc portion of an Ig molecule.

14 30. The method of claim 23, wherein:

15 the targeting agent comprises at least the Fc portion of an IgG molecule.

17 31. The method of claim 22, wherein:

18 the step of administering comprises encapsulating the antigen and the factor together in a  
19 single encapsulation device.

21 32. The method of claim 22, wherein:

1 the step of administering comprises encapsulating the antigen and the factor in separate  
2 encapsulation devices.

3  
4 33. The method of claim 31 or 32, wherein:

5 the step of administering the encapsulation device comprises associating the  
6 encapsulation device with a targeting agent.

7  
8 34. The method of claim 33, wherein:

9 the targeting agent is selected from the group consisting of mannose receptor ligand and  
10 the Fc receptor ligand.

11  
12 35. The method of claim 33, wherein:

13 the targeting agent comprises complement receptor ligand.

14  
15 36. The method of claim 33, wherein:

16 the targeting agent comprises DEC205.

17  
18 37. The method of claim 33, wherein:

19 the targeting agent directs the composition to particular vesicles within pAPCs.

20  
21 38. The method of claim 33, wherein:

the targeting agent comprises at least the Fc portion of an Ig molecule.

39. The method of claim 33, wherein:

the targeting agent comprises at least the Fc portion of an IgG molecule.

40. The method of claim 22, wherein:

the step of administering comprises providing antigen and factor that are covalently linked to one another.

41. The method of claim 22, wherein:

the step of administering comprises providing antigen and factor that are associated with one another by means of an interaction selected from the group consisting of hydrogen bonds: van der Waals interactions, hydrophobic interactions, and combinations thereof.

42. The method of claim 11, wherein:

the step of administering the antigen comprises administering a modified antigen.

43. The method of claim 42, wherein:

the modified antigen is substantially identical to a naturally-occurring antigen that contains at least one IgE binding site, but differs from that naturally-occurring antigen in that the modified antigen is missing at least one of the IgE binding sites.



1 44. The method of claim 1, wherein:  
2 the antigen comprises an autoantigen;  
3 the step of identifying an individual comprises identifying an individual who has  
4 mounted an undesirable auto-immune response against the antigen; and  
5 the factor is selected to bias the individual's immune response to the antigen away from a  
6 Th1 response.

7  
8 45. The method of claim 44, wherein  
9 the step of administering comprises administering a Th2 stimulating cytokine

10  
11 46. The method of claim 44, wherein:  
12 the step of administering comprises administering IL-4.

13  
14 47. The method of claim 45, wherein:  
15 the step of administering comprises delivering the IL-4 to the vicinity of responding T  
16 cells.

17  
18 48. The method of claim 44, wherein:  
19 the step of administering comprises administering one or more Th2 inducing agents

20  
21 49. The method of claim 44, wherein:

1 the step of administering comprises administering an agent that induces IL-4 expression.

2 *Sub B*

3 50. A method of modulating an immune system response to an antigen, the method  
4 comprising steps of:

5 isolating from an individual one or more pAPC selected from the group consisting of:  
6 mature pAPC, immature pAPC, and precursors to pAPC;

7 exposing the isolated cells to an antigen so that pAPC displaying the antigen are  
8 generated, and a pre-determined set of cytokines is expressed.

9  
10 51. The method of claim 50, further comprising:  
11 administering the antigen-exposed pAPC to a subject whose immune response to the  
12 antigen is to be modulated.

13  
14 52. The method of claim 51, wherein:  
15 the antigen-exposed pAPC are mature pAPC.

16  
17 53. The method of claim 51, wherein:  
18 the antigen-exposed pAPC are immature pAPC

19  
20 54. The method of claim 51, wherein:

1 the pAPC are selected from the group consisting of dendritic cells, B cells, and  
2 macrophages.

3 *Sub C 2*  
4 55. The method of claim 51, wherein:  
5 the pAPC are dendritic cells.  
6

7 56. The method of claim 51, wherein:  
8 the step of isolating comprises isolating immature dendritic cells from an individual; and  
9 maturing the immature cells *in vitro* by exposure to one or more compounds selected  
10 from the group consisting of: GM-CSF, IL-3, and IL-4.  
11

12 57. The method of claim 53, wherein:  
13 the step of maturing is performed concurrently with the step of exposing to antigen.  
14

15 58. The method of claim 50, wherein:  
16 the pre-determined set of cytokines is selected from the group consisting of Th1  
17 cytokines and Th2 cytokines.  
18

19 59. The method of claim 57, wherein:  
20 the Th1 cytokines are selected from the group consisting of IFN $\alpha$ , and/or IFN $\gamma$  and the  
21 Th2 cytokines are selected from the group consisting of IL-4 and IL-5, etc.

1 60. The method of claim 50, wherein:

2 the step of exposing the isolated cells to an antigen comprises exposing the cells to a  
3 crude antigen preparation.

4  
5 61. The method of claim 50, wherein:

6 the step of exposing the isolated cells to an antigen comprises exposing the cells  
7 substantially pure antigen.

8  
9 62. The method of claim 50, wherein:

10 the antigen is a polypeptide antigen; and

11 the step of exposing the isolated cells to antigen comprises exposing the cells to a gene  
12 encoding the antigen, so that the gene becomes expressed within the cells.

13  
14 63. The method of claim 50, wherein:

15 the step of exposing the cells to antigen comprises contacting the cells with an antigen  
16 that is associated with a targeting agent.

17  
18 64. The method of claim 50, wherein:

19 the step of exposing the isolated cells to an antigen further comprises exposing the cells  
20 to a composition comprising a factor selected from the group consisting of cytokines and

1 inducing agents, which factor is selected to bias an immune response in a subject away from a  
2 Th1 or a Th2 response in a pre-determined manner.

3  
4 65. The method of claim 64, wherein:

5 the step of exposing comprises exposing the cells to one or more Th1 inducing agents.

6  
7 66. The method of claim 65, wherein:

8 the Th1 inducing agents are selected from the group consisting of LPS, CD40, CD40  
9 ligand, BCGs, oligonucleotides containing CpG motifs, TNF $\alpha$ , and microbial extracts.

10  
11 67. The method of claim 66, wherein:

12 the microbial extracts are selected from the group consisting of any *Staphylococcus*  
13 *aureus* preparation, heat killed *Listeria*, and modified cholera toxin.

14  
15 68. The method of claim 64, wherein:

16 the cytokines comprise Th1 stimulatory cytokines.

17  
18 69. The method of claim 68, wherein:

19 the cytokines are selected from the group consisting of IL-12, IL-2, IL-18, IL-1 $\beta$ ,  
20 fragments of IL-1 $\beta$ , IFN $\alpha$ , and IFN $\gamma$ .

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3

1 70. The method of claim 64, wherein:  
the step of exposing comprises exposing the cells to one or ore Th2 inducing agents.

4 71. The method of claim 70, wherein:  
5 the Th2 inducing agents are characterized by an ability to induce IL-4 expression in the  
6 pAPC.

8 72. The method of claim 64, wherein:  
9 the cytokines comprise Th2 stimulatory cytokines.

11 73. The method of claim 64, wherein:  
12 the cytokines comprise IL-4.

14 74. The method of claim 64, wherein:  
15 the factor is a polypeptide; and  
16 the step of exposing the cells to a composition comprising the factor comprises contacting  
17 the cells with a gene encoding the factor.

19 75. The method of claim 74, wherein:  
20 the gene encoding the antigen and the gene encoding the factor are coordinately  
21 regulated.

1 76. The method of claim 74, wherein:

2 the gene encoding the antigen and the gene encoding the factor are provided on the same  
3 nucleic acid molecule.

4  
5 77. The method of claim 76, wherein:

6 the gene encoding the antigen and the gene encoding the factor are linked together so that  
7 a fusion protein is encoded.

8  
9 78. The method of claim 74, wherein:

10 the gene encoding the antigen and the gene encoding the factor are provided on separate  
11 nucleic acid molecules.

12  
13 79. The method of claim 64, wherein:

14 the one or both of the antigen and factor are associated with a targeting agent.

15  
16 80. The method of claim 79, wherein:

17 the association with the targeting agent occurs by means of an interaction selected from  
18 the group consisting of covalent bonds, hydrogen bonds, van der Waals interactions,  
19 hydrophobic interactions, and combinations thereof.

20  
21 81. The method of claim 79, wherein:

1 the targeting agent is selected from the group consisting of mannose receptor ligand and  
2 the Fc receptor ligand.

3  
4 82. The method of claim 79, wherein:  
5 the targeting agent comprises complement receptor ligand.

6  
7 83. The method of claim 79, wherein:  
8 the targeting agent comprises DEC205.

9  
10 84. The method of claim 79, wherein:  
11 the targeting agent is capable of targeting to intracellular vesicles within pAPCs.

12  
13 85. The method of claim 79, wherein:  
14 the targeting agent comprises at least the Fc portion of an Ig molecule.

15  
16 86. The method of claim 79, wherein:  
17 the targeting agent comprises at least the Fc portion of an IgG molecule.

18  
19 87. The method of claim 50, wherein:  
20 the antigen is encapsulated.



1 88. The method of claim 64, wherein:  
2 the step of exposing comprises providing the antigen and factor together in an  
3 encapsulation device.

4 *Suh*  
5 *B<sup>3</sup>* 89. The method of claim 64, wherein:  
6 the step of administering comprises providing the antigen and the factor in separate  
7 encapsulation devices.

8  
9 90. The method of claim 87, 88, or 89, wherein:  
10 the step of exposing comprises exposing the cells to the encapsulation device in  
11 association with a targeting agent.

12  
13 91. The method of claim 90, wherein:  
14 the targeting agent is selected from the group consisting of mannose receptor ligand and  
15 the Fc receptor ligand.

16  
17 92. The method of claim 90, wherein:  
18 the targeting agent comprises complement receptor ligand.

19  
20 93. The method of claim 90, wherein:  
21 the targeting agent comprises DEC205.

1 94. The method of claim 90, wherein:

2 the targeting agent is capable of targeting to particular vesicles within pAPCs.

3  
4 95. The method of claim 90, wherein:

5 the targeting agent comprises at least the Fc portion of an Ig molecule.

6  
7 96. The method of claim 90, wherein:

8 the targeting agent comprises at least the Fc portion of an IgG molecule.

9  
10 97. The method of claim 64, wherein:

11 the step of exposing comprises providing antigen and factor that are associated with one  
12 another by means of an interaction selected from the group consisting of: covalent bonds,  
13 hydrogen bonds, van der Waals interactions, hydrophobic interactions, and combinations thereof.

14  
15 98. The method of claim 50, wherein:

16 the step of exposing the antigen comprises exposing the cells to a modified antigen.

17  
18 99. The method of claim 64, wherein:

19 the antigen comprises an autoantigen;

20 the factor is selected to bias the immune response to the antigen away from a Th1

21 response.

1 100. The method of claim 99, wherein:

2 the factor comprises a Th2 inducing agent.

3  
4 101. The method of claim 99, wherein

5 the factor comprises an agent that induces IL-4 expression in the pAPC.

6  
7 102. The method of claim 64, wherein:

8 the antigen comprises an allergen; and

9 the factor is selected to bias the immune response to the antigen away from a Th2  
10 response.

11  
12 103. The method of claim 102, wherein:

13 the factor comprises a Th1 inducing agent.

14  
15 104. The method of claim 102, wherein:

16 the factor is selected from the group consisting of LPS, CD40, CD40 ligand, BCGs,  
17 oligonucleotides containing CpG motifs,  $\text{TNF}\alpha$ , and microbial extracts.

18  
19 105. The method of claim 104, wherein:

20 the microbial extracts are selected from the group consisting of any *Staphylococcus*  
21 *aureus* preparation, heat killed *Listeria*, and modified cholera toxin.

1 106. The method of claim 51, wherein:

2 the step of administering further comprises administering a cytokine selected from the  
3 group consisting of Th1 stimulatory cytokines and Th2 stimulatory cytokines to the subject.

5 107. The method of claim 106, wherein:

6 the Th1 stimulatory cytokines are selected from the group consisting of IL-12, IL-2, IL-  
7 18, IL-1 $\beta$ , fragments of IL-1 $\beta$ , IFN $\alpha$ , and IFN $\gamma$  and the Th2 stimulatory cytokines are selected  
8 from the group consisting of IL-4.

9 *Suh*  
10 *B4* 108. The method of claim 51 or claim 101, further comprising:

11 administering antigen to the subject.

13 109. A method of modulating an immune system response to an antigen, the method  
14 comprising steps of:

15 isolating from an individual one or more APC selected from the group consisting of:  
16 mature pAPC, immature pAPC, and precursors to pAPC;

17 exposing the isolated cells to an antigen so that mature pAPC displaying the antigen are  
18 generated; and

19 contacting the antigen-exposed pAPC with T cells so that a pre-determined T-cell  
20 response is inhibited.

1 110. The method of claim 109, wherein:  
2 the step of exposing is performed under conditions selected so that mature pAPC  
3 displaying antigen is a produced and a pre-determined set of cytokines, selected from the group  
4 consisting of Th1 cytokines and Th2 cytokines, is expressed.

5  
6 111. The method of claim 109 wherein:  
7 the pre-determined T cell response is selected from the group consisting of: a Th1  
8 response and a Th2 response.

9  
10 112. The method of claim 111, wherein:  
11 the Th1 or Th2 response is inhibited through induction of an opposing Th2 or Th1  
12 response.

13  
14 113. The method of claim 109, wherein:  
15 the step of contacting comprises contacting the antigen-exposed pAPC with T cells in the  
16 presence of one or more Th1 stimulating cytokines, so that a Th2 response is inhibited.

17  
18 114. The method of claim 109, wherein:  
19 the step of contacting comprises contacting the antigen-exposed pAPC with T cells in the  
20 presence of one or more Th1 stimulating cytokines selected from the group consisting of

1 selected from the group consisting of IL-12, IL-2, IL-18, IL-1 $\beta$ , fragments of IL-1 $\beta$ , IFN $\alpha$ , and  
2 IFN $\gamma$ .

3  
4 115. The method of claim 109, wherein:

5 the step of contacting comprises contacting the antigen-exposed pAPC with T cells in the  
6 presence of a Th1 inducing agent, so that the expression of or more Th1 cytokines is induced and  
7 a Th2 response is inhibited in the T cells.

8 *Suh*  
9 *B<sup>5</sup>* 116. The method of claim 109, wherein:

10 the step of contacting comprises contacting the antigen-exposed pAPC with T cells in the  
11 presence of a Th1 inducing agent selected from the group consisting of selected from the group  
12 consisting of LPS, CD40, CD40 ligand, BCGs, oligonucleotides containing CpG motifs, TNF $\alpha$ ,  
13 and microbial extracts, so that the expression of or more Th1 cytokines is induced and a Th2  
14 response is inhibited in the T cells.

15  
16 117. The method of claim 116, wherein:

17 the microbial extracts are selected from the group consisting of any *Staphylococcus*  
18 *aureus* preparation, heat killed *Listeria*, and modified cholera toxin.

19  
20 118. The method of claim 109, wherein:

1 the step of contacting comprises contacting the mature pAPC displaying antigen with T  
2 cells in the presence of one or more Th2 stimulating cytokines

3  
4 119. The method of claim 109, wherein:

5 the step of contacting comprises contacting the mature pAPC displaying antigen with T  
6 cells in the presence of one or more cytokines selected from the group consisting of IL-4, so that  
7 a Th1 response is inhibited.

8  
9 120. The method of claim 109, wherein:

10 the step of contacting comprises contacting the mature pAPC displaying antigen with T  
11 cells in the presence of one or more Th2 inducing agents.

12  
13 121. The method of claim 109, wherein:

14 the step of contacting comprises contacting the mature pAPC displaying antigen with T  
15 cells in the presence of one or more agents selected to induce expression of IL-4 in the  
16 responding T cells..

17  
18 122. The method of claim 109, wherein:

19 the pAPC are selected from the group consisting of dendritic cells, B cells, and  
20 macrophages.

1 123. The method of claim 109, wherein:

2 the pAPC are dendritic cells.

4 124. The method of claim 123, wherein:

5 the step of isolating comprises isolating immature dendritic cells from an individual; and

6 maturing the immature cells *in vitro* by exposure to one or more cytokines selected from  
7 the group consisting of: GM-CSF, IL-3, and IL-4.

9 125. The method of claim 123, wherein:

10 the step of maturing is performed concurrently with the step of exposing to antigen.

12 126. The method of claim 109, wherein:

13 the step of exposing the isolated cells to an antigen comprises exposing the cells to a  
14 crude antigen preparation.

16 127. The method of claim 109, wherein:

17 the step of exposing the isolated cells to an antigen comprises exposing the cells to  
18 substantially pure antigen.

20 128. The method of claim 109, wherein:



1 the step of exposing the isolated cells to antigen comprises exposing the cells to a gene  
2 encoding the antigen, so that the gene becomes expressed within the cells.

3  
4 129. The method of claim 125, wherein:

5 the step of exposing further comprises exposing the cells to a factor selected from the  
6 group consisting of cytokines and inducing agents.

7  
8 130. The method of claim 129, wherein:

9 the factor is a polypeptide and the step of exposing comprises contacting the cells with a  
10 gene encoding the factor.

11  
12 131. The method of claim 130, wherein:

13 the antigen is a polypeptide and the step of exposing comprises contacting the cells with a  
14 gene encoding the antigen

15  
16 132. The method of claim 131, wherein:

17 the gene encoding the antigen and the gene encoding the factor are coordinately  
18 regulated.

19  
20 133. The method of claim 130, wherein:

1 the gene encoding the antigen and the gene encoding the factor are provided on the same  
2 nucleic acid molecule.

3  
4 134. The method of claim 132, wherein:

5 the gene encoding the antigen and the gene encoding the factor are linked to one another  
6 so that a fusion protein is encoded.

7  
8 135. The method of claim 132, wherein:

9 the gene encoding the antigen and the gene encoding the factor are provided on separate  
10 nucleic acid molecules.

11  
12 136. The method of claim 109 wherein:

13 the antigen is provided in association with a targeting agent.

14  
15 137. The method of claim 129, wherein:

16 one or both of the antigen and factor is provided in association with a targeting agent.

17  
18 138. The method of claim 136 or claim 137, wherein:

19 the association with the targeting agent occurs by means of an interaction selected from  
20 the group consisting of covalent bonds, hydrogen bonds, van der Waals interactions,  
21 hydrophobic interactions, and combinations thereof.

- 1 139. The method of claim 136 or claim 137, wherein:  
2 the targeting agent is selected from the group consisting of mannose receptor ligand and  
3 the Fc receptor ligand.  
4
- 5 140. The method of claim 136 or claim 137, wherein:  
6 the targeting agent comprises complement receptor ligand.  
7
- 8 141. The method of claim 136 or claim 137, wherein:  
9 the targeting agent comprises DEC205.  
10
- 11 142. The method of claim 136 or claim 137, wherein:  
12 the targeting agent is capable of targeting to particular vesicles within pAPCs.  
13
- 14 143. The method of claim 136 or claim 137, wherein:  
15 the targeting agent comprises at least the Fc portion of an Ig molecule.  
16
- 17 144. The method of claim 143, wherein:  
18 the targeting agent comprises at least the Fc portion of an IgG molecule.  
19
- 20 145. The method of claim 109, wherein:  
21 the step of exposing comprises providing the antigen in an encapsulation device.

1 146. The method of claim 129, wherein:

2 one or both of the antigen and factor is encapsulated.

3

4 147. The method of claim 129, wherein:

5 the antigen and factor are provided together as a single composition.

6

7 148. The method of claim 147, wherein:

8 the antigen and factor are provided encapsulated together in a single encapsulation  
9 device.

10

11 149. The method of claim 145, 146, or claim 148, wherein:

12 the encapsulation device is associated with a targeting agent.

13

14 150. The method of claim 149, wherein:

15 the targeting agent is selected from the group consisting of mannose receptor ligand and  
16 the Fc receptor ligand.

17

18 151. The method of claim 149, wherein:

19 the targeting agent comprises complement receptor ligand.

20

21 152. The method of claim 149, wherein:

1 the targeting agent comprises DEC205.

2  
3 153. The method of claim 149, wherein:

4 the targeting agent is capable of targeting to intracellular vesicles within pAPCs.

5  
6 154. The method of claim 149, wherein:

7 the targeting agent comprises at least the Fc portion of an Ig molecule.

8  
9 155. The method of claim 149, wherein:

10 the targeting agent comprises at least the Fc portion of an IgG molecule.

11  
12 156. The method of claim 129, wherein:

13 the step of exposing comprises providing antigen and factor that are associated with one  
14 another by means of an interaction selected from the group consisting of: covalent bonds,  
15 hydrogen bonds, van der Waals interactions, hydrophobic interactions, and combinations thereof.

16  
17 157. The method of claim 109, wherein:

18 the step of exposing the antigen comprises exposing the cells to a modified antigen.

19  
20 158. The method of claim 149, wherein:

21 the antigen comprises an autoantigen; and

1 the pre-determined set of cytokines comprises Th2 cytokines.

2

3 159. The method of claim 149, wherein:

4 the pre-determined set of cytokines comprises IL-4.

5

6

7 160. A method of treating allergy, the method comprising steps of:

8 identifying an individual who is allergic to an antigen;

9 providing a composition of pAPC displaying the antigen; and

10 contacting the composition with T cells of the individual under conditions that inhibit a

11 Th2 response to the antigen.

12

13 161. The method of claim 160, wherein:

14 the mature pAPC are selected for their expression of Th1 cytokines.

15

16 162. The method of claim 160, wherein:

17 the pAPC are selected from the group consisting of dendritic cells, B cells, and

18 macrophages.

19

20 163. The method of claim 161, wherein:

21 the pAPC are dendritic cells.

1 164. The method of claim 160, wherein:  
2 the step of providing comprises:  
3 isolating from an individual one or more cells selected from the group consisting  
4 of mature pAPC, immature pAPC, and precursors to pAPC; and  
5 exposing the isolated cells to the antigen.  
6

7 165. The method of claim 164, wherein:  
8 the step of exposing the isolated cells to the antigen further comprises exposing the  
9 isolated cells to a factor selected from the group consisting of cytokines and inducing agents.  
10

11 166. The method of claim 165, wherein:  
12 the factor comprises an inducing agent that induces expression of one or more Th1  
13 stimulating cytokines in the pAPC.  
14

15 167. The method of claim 165 wherein:  
16 the antigen and factor are provided together as part of a single composition.  
17

18 168. The method of claim 165, wherein:  
19 one or both of the antigen and factor is associated with a targeting agent.  
20

21 169. The method of claim 164, wherein:

1 the antigen is associated with a targeting agent.

2  
3 170. The method of claim 167, wherein:

4 the antigen and factor are encapsulated together in an encapsulation device.

5  
6 171. The method of claim 164, wherein

7 the antigen is encapsulated.

8  
9 172. The method of claim 165, wherein:

10 one or both of the antigen and factor is encapsulated.

11  
12 173. The method of claim 165, wherein:

13 the antigen and factor are both encapsulated.

14  
15 174. The method of claim 173, wherein:

16 the encapsulation device is associated with a targeting agent.

17  
18 175. The method of claim 164, wherein:

19 the step of exposing the isolated cells to antigen comprises exposing the cells to a crude  
20 preparation of antigen.



1 176. The method of claim 164, wherein:

2 the step of exposing the isolated cells to an antigen comprises exposing the cells  
3 substantially pure antigen.

4  
5 177. The method of claim 164, wherein:

6 the antigen is a polypeptide antigen; and

7 the step of exposing the isolated cells to antigen comprises exposing the cells to a gene  
8 encoding the antigen, so that the gene becomes expressed within the cells.

9  
10 178. The method of claim 164, wherein:

11 the factor is a polypeptide and the step of exposing comprises exposing the cells to a gene  
12 encoding the factor.

13  
14 179. The method of claim 178, wherein:

15 the antigen is a polypeptide antigen; and

16 the step of exposing the isolated cells to antigen comprises exposing the cells to a gene  
17 encoding the antigen, so that the gene becomes expressed within the cells.

18  
19 180. The method of claim 179, wherein:

20 the antigen gene and the factor gene are coordinately regulated.

21

1 181. The method of claim 179, wherein:  
2 the antigen gene and the factor gene are provided on the same nucleic acid molecule.  
3

4 182. The method of claim 181, wherein:  
5 the antigen gene and the factor gene are linked to one another so that a single fusion  
6 protein is encoded.  
7

8 183. The method of claim 179, wherein:  
9 the antigen gene and the factor gene are provided on separate nucleic acid molecules.  
10

11 184. The method of any one of claims 168, 169, or 174, wherein:  
12 the association with the targeting agent occurs through an interaction selected from the  
13 group consisting of covalent bonds, hydrogen bonds, van der Waals interactions, hydrophobic  
14 interactions, and combinations thereof.  
15

16 185. The method of any one of claims 168, 169, or 174, wherein:  
17 the targeting agent is selected from the group consisting of mannose receptor ligand and  
18 the Fc receptor ligand.  
19

20 186. The method of any one of claims 168, 169, or 174, wherein:  
21 the targeting agent comprises complement receptor ligand.

1 187. The method of any one of claims 168, 169, or 174, wherein:

2 the targeting agent comprises DEC205.

4 188. The method of any one of claims 168, 169, or 174, wherein:

5 the targeting agent is capable of targeting to intracellular vesicles within pAPCs.

7 189. The method of any one of claims 168, 169, or 174, wherein:

8 the targeting agent comprises at least the Fc portion of an Ig molecule.

10 190. The method of any one of claims 168, 169, or 174, wherein:

11 the targeting agent comprises at least the Fc portion of an IgG molecule.

13 191. The method of claim 175, wherein:

14 the step of exposing comprises providing antigen and factor that are associated with one  
15 another by means of an interaction selected from the group consisting of: covalent bonds,  
16 hydrogen bonds, van der Waals interactions, hydrophobic interactions, and combinations thereof.

18 192. The method of claim 164, wherein:

19 the step of exposing the antigen comprises exposing the cells to a modified antigen.

21 193. The method of claim 192, wherein:

1 the modified antigen is substantially identical to a naturally-occurring antigen that  
2 contains at least one IgE binding site except that the modified antigen lacks at least one of the  
3 IgE binding sites.

4  
5 194. A method of treating an autoimmune disorder, the method comprising steps of:  
6 identifying an individual who is susceptible to or has mounted an undesirable immune  
7 response against an antigen;  
8 providing a composition of pAPC displaying the antigen; and  
9 contacting the composition with T cells of the individual under conditions that inhibit a  
10 Th1 response to the antigen.

11  
12 195. The method of claim 194, wherein:  
13 the step of identifying comprises identifying an individual who has previously mounted a  
14 Th1 response to the antigen.

15  
16 196. The method of claim 194, wherein:  
17 the pAPC are selected for their expression of Th2 stimulating cytokines.

18  
19 197. The method of claim 194, wherein:  
20 the pAPC are selected from the group consisting of dendritic cells, B cells, and  
21 macrophages.

1 198. The method of claim 194, wherein:

2 the pAPC are B cells.

4 199. The method of claim 194, wherein:

5 the step of providing comprises:

6 isolating from an individual one or more cells selected from the group consisting  
7 of mature pAPC, immature pAPC, and precursors to pAPC; and  
8 exposing the isolated cells to the antigen.

10 200. The method of claim 199, wherein:

11 the step of exposing the isolated cells to the antigen further comprises exposing the  
12 isolated cells to a factor selected from the group consisting of cytokines and inducing agents.

14 201. The method of claim 200, wherein:

15 the factor comprises an inducing agent that induces expression of one or more Th2  
16 cytokines.

18 202. The method of claim 200, wherein:

19 the antigen and factor are provided together as part of a single composition.

21 203. The method of claim 200, wherein:

1 one or both of the antigen and factor is associated with a targeting agent.

2  
3 204. The method of claim 199, wherein:

4 the antigen is associated with a targeting agent.

5  
6 205. The method of claim 203, wherein:

7 the antigen and factor are encapsulated together in an encapsulation device.

8  
9 206. The method of claim 199, wherein

10 the antigen is encapsulated.

11  
12 207. The method of claim 200, wherein:

13 the antigen and factor are both encapsulated.

14  
15 208. The method of claim 205, 206, or 207 wherein:

16 the encapsulation device is associated with a targeting agent.

17  
18 209. The method of claim 200, wherein:

19 the step of exposing the isolated cells to antigen comprises exposing the cells to a crude  
20 preparation of antigen.

1 210. The method of claim 200, wherein:

2 the step of exposing the isolated cells to an antigen comprises exposing the cells  
3 substantially pure antigen.  
4

5 211. The method of claim 199, wherein:

6 the antigen is a polypeptide antigen; and  
7 the step of exposing the isolated cells to antigen comprises exposing the cells to a gene  
8 encoding the antigen, so that the gene becomes expressed within the cells.  
9

10 212. The method of claim 200, wherein:

11 the factor is a polypeptide and the step of exposing comprises exposing the cells to a gene  
12 encoding the factor.  
13

14 213. The method of claim 212, wherein:

15 the antigen is a polypeptide antigen; and  
16 the step of exposing the isolated cells to antigen comprises exposing the cells to a gene  
17 encoding the antigen, so that the gene becomes expressed within the cells.  
18

19 214. The method of claim 213, wherein:

20 the antigen gene and the factor gene are coordinately regulated.  
21

1 215. The method of claim 213, wherein:

2 the antigen gene and the factor gene are provided on the same nucleic acid molecule.

3  
4 216. The method of claim 215, wherein:

5 the antigen gene and the factor gene are linked to one another so that a single fusion  
6 protein is encoded.

7  
8 217. The method of claim 213, wherein:

9 the antigen gene and the factor gene are provided on separate nucleic acid molecules.

10  
11 218. The method of any one of claims 203, 204, or 208, wherein:

12 the association with the targeting agent occurs through an interaction selected from the  
13 group consisting of covalent bonds, hydrogen bonds, van der Waals interactions, hydrophobic  
14 interactions, and combinations thereof.

15  
16 219. The method of any one of claims 203, 204, or 208, wherein:

17 the targeting agent is selected from the group consisting of mannose receptor ligand and  
18 the Fc receptor ligand.

19  
20 220. The method of any one of claims 203, 204, or 208, wherein:

21 the targeting agent comprises complement receptor ligand.



1 221. The method of any one of claims 203, 204, or 208, wherein:

2 the targeting agent is capable of targeting to intracellular vesicles within pAPCs.

3  
4 222. The method of any one of claims 203, 204, or 208, wherein:

5 the targeting agent comprises at least the Fc portion of an Ig molecule.

6  
7 223. The method of any one of claims 203, 204, or 208, wherein:

8 the targeting agent comprises at least the Fc portion of an IgG molecule.

9  
10 224. The method of claim 200, wherein:

11 the step of exposing comprises providing antigen and factor that are associated with one  
12 another by means of an interaction selected from the group consisting of covalent bonds, van der  
13 Waals interactions, hydrophobic interactions, and combinations thereof.

14  
15 225. The method of claim 199, wherein:

16 the step of exposing the antigen comprises exposing the cells to a modified antigen.

17  
18 226. The method of claim 225, wherein:

19 the modified antigen is substantially identical to a naturally-occurring antigen that  
20 contains at least one IgE binding site except that the modified antigen lacks at least one of the  
21 IgE binding sites.

1 227. A composition for modulating an immune system response to an antigen in an individual  
2 comprising:

3 an antigen; and

4 at least one factor selected from the group consisting of cytokines and inducing  
5 agents.

6  
7 228. The composition of claim 227, wherein:

8 the factor comprises a Th1 stimulating cytokine.

9  
10 229. The composition of claim 227, wherein:

11 the factor is selected from the group consisting of IL-12, IL-2, IL-18, IL-1 $\beta$ , fragments of  
12 IL-1 $\beta$ , IFN $\alpha$ , and IFN $\gamma$ .

13  
14 230. The composition of claim 227, wherein:

15 the factor comprises a Th2 stimulating cytokine.

16  
17 231. The composition of claim 227, wherein:

18 the factor comprises IL-4.

19  
20 232. The composition of claim 227, wherein:

21 the factor comprises a Th1 inducing agent.

1 233. The composition of claim 227, wherein:

2 the factor is selected from the group consisting of LPS, CD40, CD40 ligand, BCGs,  
3 oligonucleotides containing CpG motifs, TNF $\alpha$ , and microbial extracts.

4  
5 234. The composition of claim 233, wherein:

6 the microbial extracts are selected from the group consisting of any *Staphylococcus*  
7 *aureus* preparation, heat killed *Listeria*, and modified cholera toxin.

8  
9 235. The composition of claim 227, wherein:

10 the factor comprises a Th2 inducing agent.

11  
12 236. The composition of claim 227, wherein:

13 the factor comprises an agent that induces IL-4 expression.

14  
15 237. The composition of claim 227, wherein:

16 the antigen comprises a crude antigen preparation.

17  
18 238. The composition of claim 227, wherein:

19 the antigen comprises a substantially pure antigen

20  
21 239. The composition of claim 227, further comprising:

1 an encapsulation device surrounding the antigen and factor.

2  
3 240. The composition of claim 227 or claim 228, further comprising:  
4 a targeting agent.

5  
6 241. The composition of claim 240, wherein:  
7 the targeting agent is associated with the composition through a covalent or a non-  
8 covalent interaction.

9  
10 242. The composition of claim 240, wherein:  
11 the targeting agent is selected from the group consisting of mannose receptor ligand and  
12 the Fc receptor ligand.

13  
14 243. The composition of claim 239, wherein:  
15 the targeting agent comprises complement receptor ligand.

16  
17 244. The composition of claim 239, wherein:  
18 the targeting agent comprises DEC205.

19  
20 245. The composition of claim 239, wherein:  
21 the targeting agent is capable of targeting to intracellular vesicles within pAPCs.

1 246. The composition of claim 239, wherein:

2 the targeting agent comprises at least the Fc portion of an Ig molecule.

4 247. The composition of claim 239, wherein:

5 the targeting agent comprises at least the Fc portion of an IgG molecule.

7 248. The composition of claim 227, wherein:

8 the antigen and factor are covalently linked to one another.

10 249. The composition of claim 227, wherein:

11 the antigen and factor that are associated with one another by means of an interaction  
12 selected from the group consisting of: hydrogen bonds, van der Waals interaction, hydrophobic  
13 interaction, and combinations thereof.

15 250. The composition of claim 227, wherein:

16 the antigen comprises a modified antigen.

18 251. The composition of claim 227, which composition is formulated for oral administration.

20 252. The composition of claim 227, which composition is formulated for inhalation.

1 253. The composition of claim 227, which composition is formulated for injection.

2  
3 254. A composition for modulating an immune system response to an antigen in an individual  
4 comprising:

5 one or more pAPC displaying an antigen and expressing a predetermined collection of  
6 cytokines, selected from the group consisting of Th1 cytokines and Th2 cytokines; and  
7 at least one factor selected from the group consisting of cytokines and inducing agents.

8  
9 255. The composition of claim 254, wherein:

10 the pAPC are selected from the group consisting of dendritic cells, B cells, and  
11 macrophages.

12  
13 256. The composition of claim 255, wherein

14 the pAPC are dendritic cells.

15  
16 257. The composition of claim 255, wherein:

17 the dendritic cells are prepared by a process comprising steps of:

18 isolating immature dendritic cells from an individual; and

19 maturing the isolated cells in vitro by exposure to one or more cytokines selected  
20 from the group consisting of: GM-CSF, IL-3, and IL-4.

1 258. The composition of 257, wherein:

2 the maturing is performed in the presence of the antigen.

3  
4 259. The composition of claim 254, wherein:

5 the factor comprises a Th1 stimulating cytokine.

6  
7 260. The composition of claim 254, wherein:

8 the factor is selected from the group consisting of IL-12, IL-2, IL-18, IL-1 $\beta$ , fragments of  
9 IL-1 $\beta$ , IFN $\alpha$ , and IFN $\gamma$

10  
11 261. The composition of claim 254, wherein:

12 the factor comprises a Th1 inducing agent.

13  
14 262. The composition of claim 254, wherein:

15 the factor is selected from the group consisting of LPS, CD40, CD40 ligand, BCGs,  
16 oligonucleotides containing CpG motifs, TNF $\alpha$ , and microbial extracts.

17  
18 263. The method of claim 262, wherein:

19 the microbial extracts are selected from the group consisting of any *Staphylococcus*  
20 *aureus* preparation, heat killed *Listeria*, and modified cholera toxin.

1 264. The composition of claim 254, wherein:

2 the factor comprises a Th2 stimulating cytokine.

3  
4 265. The composition of claim 254, wherein:

5 the factor comprises IL-4.

6  
7 266. The composition of claim 254, wherein:

8 the factor comprises a Th2 inducing agent.

9  
10 267. The composition of claim 254, wherein:

11 the factor comprises an agent that induces IL-4 expression.

12  
13 268. The composition of claim 254, wherein:

14 the factor comprises an agent that inhibits IL-12 expression.

15  
16 269. The composition of claim 258, wherein:

17 the antigen comprises a crude antigen preparation.

18  
19 270. The composition of claim 254, wherein:

20 the antigen comprises a substantially pure antigen.



1 271. The composition of claim 254, wherein:

2 the antigen comprises a modified antigen.

3  
4 272. A composition comprising:

5 a gene encoding an antigen; and

6 a gene encoding at least one factor selected from the group consisting of cytokines and  
7 inducing agents.

8  
9 273. The composition of claim 272, wherein:

10 the antigen gene and the factor gene are coordinately regulated.

11  
12 274. The composition of claim 272, wherein:

13 the antigen gene and the factor gene are on the same nucleic acid molecule.

14  
15 275. The composition of claim 272, wherein:

16 the antigen gene and the factor gene are linked together so that a single polypeptide is  
17 encoded.

18  
19 276. The composition of claim 272, wherein:

20 the antigen gene and the factor gene are provided on separate nucleic acid molecules.

1 277. The composition of claim 272, further comprising an encapsulation device surrounding  
2 the genes.

3  
4 278. The composition of claim 272 or claim 277, further comprising:  
5 a targeting agent selected for its ability to localize the composition in the vicinity of  
6 pAPC.

7  
8 279. The composition of claim 272, which composition is formulated for oral administration.

9  
10 280. The composition of claim 272, which composition is formulated for inhalation.

11  
12 281. The composition of claim 272, which composition is formulated for injection.